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Indian Standard

GUIDE FOR EVALUATION OF MEDICAL DEVICES FOR BIOLOGICAL HAZARDS

PART 8 METHOD OF TEST FOR SKIN IRRITATION OF EXTRACTS FROM MEDICAL DEVICES

भारतीय मानक

जैव-वैज्ञानिक खतरों के लिए चिकित्सीय युक्तियों के मूल्यांकन की मार्गदर्शिका

भाग 8 चिकित्सीय युक्तियों के निष्कर्षों से उत्पन्न त्वचा-क्षोभ की परीक्षण पद्धति

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DESCRIPTORS : EVALUATION OF MEDICAL DEVICES. BIOLOGICAL HAZARDS. SKIN IRRITATION. EXTRACTS FROM MEDICAL DEVICES.

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October 1989

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Medical Glass Instruments and Appliances Sectional Committee, CPDC 12

FOREWORD

This Indian Standard (Part 8) was adopted by the Bureau of Indian Standards on 14 September 1988, after the draft finalized by the Medical Glass Instruments and Appliances Sectional Committee had been approved by the Consumer Products and Medical Instruments Division Council.

This part (Part 8) of the standard is one of the series of methods of test for assessing the biological hazards of medical devices that directly come in contact with body tissues or substances that are to be introduced into the body by means other than oral.

Part 2 provides guidance on the selection of recommended methods of test for the initial assessment of biological hazards in medical devices. This part of the standard describes the method of test for skin irritation of extracts from medical devices.

This standard is proposed to be published in 12 parts. Other parts are as follows:

Part 1 Terminology

Part 2 Selection of biological methods of test

Part 3 Method of testing by tissue implantation

Part 4 Method of test for systemic toxicity: Assessment of acute toxicity of extracts from medical devices

Part 5 Method of test for intracutaneous reactivity of extracts from medical devices

Part 6 Method of test for systemic toxicity: Assessment of pyrogenicity in rabbits of extracts from medical devices

Part 7 Methods of test for sensitization: Assessment of potential of medical devices to produce delayed contact dermatitis

Part 9 Method of test for skin irritation of solid medical devices

Part 10 Method of tests for dental materials

Part 11 Method of tests for eye irritation

Part 12 Methods of test for toxicity to cells in culture of extracts from medical devices

In the preparation of this standard, assistance has been derived from BS 5736 : Part 7 : 1983 'Evaluation of medical devices for biological hazards: Part 7 Methods of test for skin irritation of extracts from medical devices', issued by the British Standards Institution, UK.

Indian Standard

GUIDE FOR EVALUATION OF MEDICAL DEVICES FOR BIOLOGICAL HAZARDS

PART 8 METHOD OF TEST FOR SKIN IRRITATION OF EXTRACTS FROM MEDICAL DEVICES

1 SCOPE

1.1 This standard describes a test method designed to assess the irritation of skin by leachable endogenous or extraneous substances present in or on a medical device. This method specifies the use of both polar and non-polar solvents to obtain extracts of devices. These extracts are administered by application to the skin for five consecutive days.

1.2 This method of test is recommended for the initial assessment of devices in Group C, D and E_2 (*see* Part 2 of this standard), that is:

a) *Category C* — Those intended for short-term (short-term covers a period from a few minutes to several weeks continuous use) use within the body or in contact with the mucosal surfaces, such as, tracheal tubes, urinary catheters, intravenous canulae;

b) *Category D* — Those intended to be used in contact with the skin, such as, splints;

c) *Category E_2* — Those intended to be used to contain or administer substances by means of routes other than those in Group E_1, such as, eyedrop containers.

2 DEFINITIONS

2.0 For the purpose of this standard, the following definitions shall apply.

2.1 Device, Medical Device

Any item used in medical treatment, diagnosis or contraception not intended to have a pharmacological action on the body.

2.2 Erythema

Tissue reaction characterized by redness at the application site.

2.3 Eschar

Tissue reaction characterized by scab formation at the application site.

2.4 Final Product

A medical device in its ready-to-use state.

2.5 Oedema

Tissue reaction characterized by swelling at the application site.

2.6 Test Material

The final product or sample of final product that is to be tested.

3 ANIMALS AND HUSBANDRY

3.1 Six albino rabbits of a single strain shall be used. They shall be healthy young adults of either sex weighing not less than 2 kg. The animals shall be caged individually and shall have free access to food and water.

4 PREPARATION OF EXTRACTS OF FINAL PRODUCTS

4.1 Test Material

4.1.1 Test material from pre-sterilized (refers to devices obtained from the manufacturer or the supplier and sterilized) devices shall be handled aseptically throughout the extraction and test procedure.

4.1.2 Test material from devices that are normally supplied non-sterile but are sterilized before use, shall be sterilized before the extraction procedure and handled aseptically throughout the extraction and test procedure.

4.1.3 Test material from devices not required to be sterile in use shall be subjected to the extraction procedure and the extracts obtained with polar solvent shall then be sterilized before administration (*see* **4.2.2.1**).

4.2 Extractants

4.2.1 *Polar Solvent*

Sterile saline solution containing 9 g/l sodium chloride.

4.2.2 *Non-Polar Solvent*

Seasame oil IP or USP, or Cotton seed oil IP or USP.

4.2.2.1 It may not be practical to sterilize the non-polar solvent. Care should be taken to minimize any possible microbial contamination.

4.3 Principles of Extraction

4.3.1 The test material shall be representative of the final product or the component of the final product, that is to be tested.

4.3.1.1 To achieve this, the test material may consist of small pieces of the final product, or one or more intact devices. For multicomponent devices, it may be appropriate to test the individual components of devices separately.

4.3.1.2 The quantity of any indogenous or extraneous substances extracted is related to the surface area of the sample (interfacial area) with which the extractant is brought into contact.

4.3.1.3 The concentration of any endogenous or extraneous substances in the extract and hence the dose delivered to the test animal depends on both the interfacial area and the final extract volume.

4.3.1.4 The interfacial area per unit volume of extract has to be taken into consideration when the dose given to test animal is related to the likely exposure of the device to man.

4.3.2 To render the test as sensitive as possible, the ratio between interfacial area and the final extract volume shall be as high as is practicable. The interfacial area per millilitre of the final extract volume shall be not less than 12·5 cm^2.

4.3.2.1 The figure of 12·5 cm^2/ml arises from the consideration of dose per unit area presented to the skin of the test animals (*see* **5.2**).

4.3.3 The technique to be used in exposing the test material to the extractant shall be selected according to the requirements of **4.3.1** and **4.3.2**.

4.3.3.1 Fragmentation of the test material may be used to increase the interfacial area.

4.3.4 Extraction conditions shall simulate as closely as possible the conditions under which the device will normally be used.

4.3.5 During the extraction, 27±3°C shall be the representative of room temperature and 37±2°C shall be the representative of body temperature.

4.3.6 The period of contact between the extractant and the test material shall be 72 h.

4.4 Procedure

4.4.1 Using the polar and the non-polar solvent as extractants, prepare in accordance with **4.1** and **4.3** sufficient volumes of extracts for administration as described in **5**.

4.4.2 In conditions identical with those used in **4.4.1**, prepare controls, using both the polar and the non-polar solvent, in the absence of the test material.

4.4.3 Sterilize the extracts obtained with the polar solvent from the unsterilized devices (*see* **4.1.3**).

4.4.4 Record for the test report, the precise conditions of extraction and, where applicable, of sterilization.

5 TEST PROCEDURE

5.1 Preparation of Animals

On the day before the test, clip the fur on the backs of six animals close to the skin to permit a sufficient distance on both sides of the spinal column for application and observation of all test sites. Only animals with healthy intact skin should be used. Immediately before the application of the extract, abrade the right hand side sites of each animal to break partially the stratum corneum.

5.2 Application of Extracts and Extractants

Apply the polar extract to six 25 mm square 4-ply gauze patches (0·5 ml per patch), one on each side of three animals as shown in Fig. 1.

5.2.1 Similarly apply the polar solvent control to each animal.

5.2.2 Cover the treatment sites with retaining dressings for 6 h. At the end of this period, remove the dressings and patches and mark the positions of the sites. Gently wash the treatment sites with warm (30 to 40°C) water to remove residual extract and blot dry.

5.2.3 Carry out these procedures at the same sites for five consecutive days.

5.2.4 Using the second set of animals, carry out these procedures using the non-polar extract and control.

5.3 Observation of Animals

Note the appearance of each application site within 1 h after removal of the dressing and immediately prior to the next application (that is, 7 h and 24 h after each application).

5.3.1 Describe and rate the skin reactions of erythema and oedema according to the rating system given in Table 1 for each application site at each time interval and record the results for the test report.

6 PRESENTATION OF RESULTS

6.1 The results shall be submitted in a test report that includes a complete record of the method of

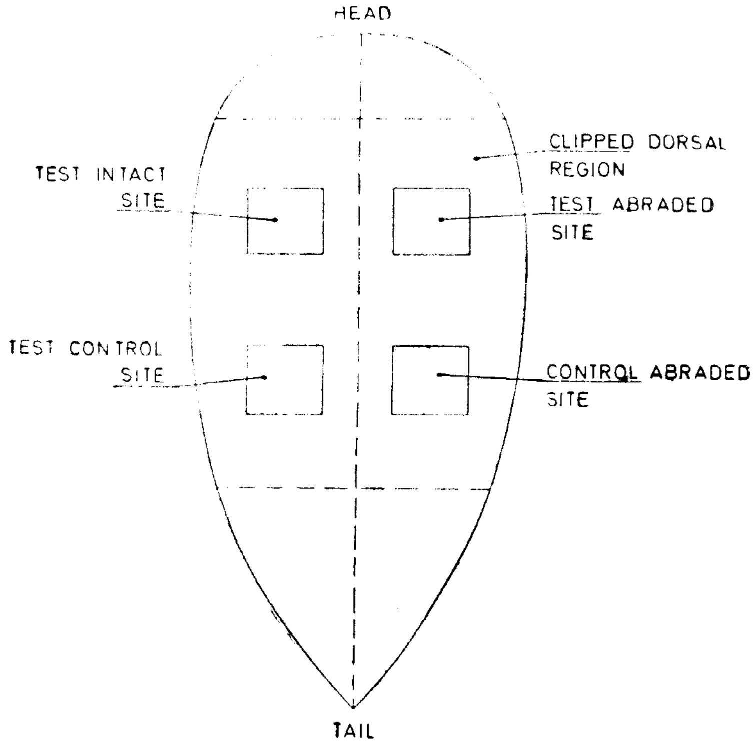

FIG. 1 LOCATIONS OF SKIN APPLICATION SITES

extraction, the procedures followed and data necessary for the assessment of results as described in 7.

7 ASSESSMENT OF RESULTS

7.0 The assessment of results should be carried out by an experienced person (preferably a toxicologist) who is aware of the conditions of use of the final product and has appropriate chemical and biological data concerning it (*see* 3.3 and 3.4 of Part 2 of this standard).

7.1 The overall assessment of the test results shall be carried out, taking into consideration any difference observed between the abraded and the intact sites, and the test and the control sites.

7.2 If the assessor considers the results to be either inconclusive or invalid, the test shall be repeated using different animals, new extracts and if necessary, different extractants.

Table 1 Rating System for Skin Reactions

(*Clause* 5.3.1)

Reaction	Numerical Rating
Erythema and Eschar Formation	
No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation	4
Oedema Formation	
No oedema	0
Very slight oedema (barely perceptible)	1
Well defined oedema (edges of area well defined by definite raising)	2
Moderate oedema (raised approximately 1 mm)	3
Severe oedema (raised more than 1 mm and extending beyond exposure area)	4

NOTE — Other adverse changes at the skin sites should be recorded and reported.

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